Patent
Attorney's Docket No. 1024637-000191

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Patent Application of

Peter Kite et al.

Application No.: 10/659,413

Filed: September 10, 2003

For: ANTISEPTIC COMPOSITIONS, METHODS AND SYSTEMS

MAIL STOP APPEAL BRIEF - PATENTS

Group Art Unit: 1617

Examiner: SHOBHA KANTAMNENI

Confirmation No.: 4621

RESPONSE TO NOTIFICATION OF NON-COMPLIANT APPEAL BRIEF

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Sir:

In response to the Notice of Non-Compliant Appeal Brief mailed November 28, 2006, attached is a copy of the Appeal Brief filed in U.S. Patent Application No. 10/313,844, stated in the Related Proceedings Appendix.

Respectfully submitted,

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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
ART UNIT	PAPER NUMBER

DATE MAILED: 11/28/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Notification of Non-Compliant Appeal Brief (37 CFR 41.37)	Application No.	Applicant(s)	
	10/659,413	KITE ET AL.	
	Examiner	Art Unit	
	KANTAMNENI, SHOBHA	1617	

--The MAILING DATE of this communication appears on the cover sheet with the correspondence address--

The Appeal Brief filed on *23 August 2006* is defective for failure to comply with one or more provisions of 37 CFR 41.37.

To avoid dismissal of the appeal, applicant must file anamended brief or other appropriate correction (see MPEP 1205.03) within **ONE MONTH or THIRTY DAYS** from the mailing date of this Notification, whichever is longer. **EXTENSIONS OF THIS TIME PERIOD MAY BE GRANTED UNDER 37 CFR 1.136.**

1. ☐ The brief does not contain the items required under 37 CFR 41.37(c), or the items are not under the proper heading or in the proper order.

2. ☐ The brief does not contain a statement of the status of all claims, (e.g., rejected, allowed, withdrawn, objected to, canceled), or does not identify the appealed claims (37 CFR 41.37(c)(1)(iii)).

3. ☐ At least one amendment has been filed subsequent to the final rejection, and the brief does not contain a statement of the status of each such amendment (37 CFR 41.37(c)(1)(iv)).

4. ☐ (a) The brief does not contain a concise explanation of the subject matter defined in each of the independent claims involved in the appeal, referring to the specification by page and line number and to the drawings, if any, by reference characters; and/or (b) the brief fails to: (1) identify, for each independent claim involved in the appeal and for each dependent claim argued separately, every means plus function and step plus function under 35 U.S.C. 112, sixth paragraph, and/or (2) set forth the structure, material, or acts described in the specification as corresponding to each claimed function with reference to the specification by page and line number, and to the drawings, if any, by reference characters (37 CFR 41.37(c)(1)(v)).

5. ☐ The brief does not contain a concise statement of each ground of rejection presented for review (37 CFR 41.37(c)(1)(vi))

6. ☐ The brief does not present an argument under a separate heading for each ground of rejection on appeal (37 CFR 41.37(c)(1)(vii)).

7. ☐ The brief does not contain a correct copy of the appealed claims as an appendix thereto (37 CFR 41.37(c)(1)(viii)).

8. ☐ The brief does not contain copies of the evidence submitted under 37 CFR 1.130, 1.131, or 1.132 or of any other evidence entered by the examiner **and relied upon by appellant in the appeal**, along with a statement setting forth where in the record that evidence was entered by the examiner, as an appendix thereto (37 CFR 41.37(c)(1)(ix)).

9. ☒ The brief does not contain copies of the decisions rendered by a court or the Board in the proceeding identified in the Related Appeals and Interferences section of the brief as an appendix thereto (37 CFR 41.37(c)(1)(x)).

10. ☐ Other (including any explanation in support of the above items):

Item 9. The attachment re: 10/313,844 stated in the Related Proceedings Appendix was not attached to the brief.

Linda Hood

LORENDA HOOD
PATENT APPEAL CENTER SPECIALIST

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Patent Application of	)	**Mail Stop:**
	)	**APPEAL BRIEF - PATENTS**
Peter KITE et al.	)	
	)	Group Art Unit: 1617
Application No.: 10/659,413	)	
	)	Examiner: Shobha Kantamneni
Filed: September 10, 2003	)	
	)	Confirmation No.: 4621
For: ANTISEPTIC COMPOSITIONS, METHODS AND SYSTEMS	)	
	)	Appeal No.: 1

APPEAL BRIEF

Mail Stop APPEAL BRIEF - PATENTS
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Sir:

This appeal is from the decision of the Office issued on February 24, 2006, finally rejecting claims 32, 34, 37, 39, 41, 42, 45-47 and 55-60, which are reproduced as the Claims Appendix of this brief.

☒ A check covering the ☐ $250.00 (2402) ☒ $500.00 (1402) Government fee is filed herewith.

☐ Charge ☐ $250.00 (2402) ☐ $500.00 (1402) to Credit Card. Form PTO-2038 is attached.

The Commissioner is hereby authorized to charge any appropriate fees under 37 C.F.R. §§1.16, 1.17, and 1.21 that may be required by this paper, and to credit any overpayment, to Deposit Account No. 02-4800.

I. Real Party in Interest

The present application is assigned to Tyco Healthcare Group LP which is the real party in interest.

II. Related Appeals and Interferences

Appellants' legal representative and assignee are aware of one other appeal or interferences which may affect or be directly affected by or have a bearing on the Board's decision in the pending appeal. The Board is directed to an Appeal and associated Appeal Brief for U.S. Patent Application Serial No. 10/313,844. A Related Proceedings Appendix is attached.

III. Status of Claims

Claims 32, 34, 37, 39, 41, 42, 45-47 and 55-60 are pending, rejected and presently appealed. A copy of the claims involved in the appeal is contained in an attached Claims Appendix.

IV. Status of Amendments

No amendments have been filed subsequent to the final rejection of February 24, 2006.

V. Summary of Claimed Subject Matter

The claimed subject matter involves antiseptic solutions comprising at least one salt of ethylene diamine tetraacetic acid (EDTA) in solution, wherein the at least one EDTA salt comprises at least one of tri-sodium and tetra-sodium EDTA at a prescribed concentration and/or pH. The inventors have discovered, unexpectedly, that certain EDTA compositions provide powerful antiseptic activities and function as broad-spectrum anti-microbial agents, as well as fungicidal agents against many strains of pathogenic yeast. EDTA compositions of the claimed subject matter are also highly effective in killing pathogenic biofilm organisms and in reducing and eliminating existing biofilms, as well as preventing biofilm formation. EDTA compositions moreover exhibit anti-protozoan activity including anti-amoebic activity. *See, e.g.,* specification page 8, lines 16-24. They are thus highly effective antiseptic compositions.

Because the EDTA compositions of the claimed subject matter have the wide spectrum antiseptic activities described above, and because they are safe for human administration and are biocompatible and non-corrosive, they have numerous applications, including applications as lock and lock flush solutions for various types of catheters, use as antiseptic agents or solutions for sanitizing a range of medical, dental and veterinary devices, instruments and other objects, surfaces, and the like. *See, e.g.,* specification page 8, lines 27-34.

The efficacy of the claimed compositions is superior to many antiseptic compositions conventionally used for these applications. The claimed compositions are additionally effective in preventing biofilm formation and substantially eliminating biofilm organisms, which many antibiotics and biocidal agents are not. The claimed compositions do *not* contribute to antibiotic resistance, which provides yet another important benefit.

Four of the appealed claims are in independent format: claims 32, 55, 56 and 57. Independent claim 32 recites an antiseptic composition comprising at least one of tri-sodium and tetra-sodium EDTA in solution at a concentration of at least 2.0% (w/v) and less than 15% (w/v) and having a pH of at least 9.5, wherein the antiseptic composition has a bactericidal effect over a broad spectrum of microbes and is packaged in a sterile, non-pyrogenic form. Independent claim 55 additionally recites that the solution is water and the antiseptic composition has an osmolarity of from 240-500 mOsM/Kg. Independent claim 57 recites an antiseptic composition comprising tri- and tetra-sodium EDTA in solution at a concentration sufficient to have antimicrobial activity and at a pH of at least 9.5, wherein the antiseptic composition has a bactericidal effect over a broad spectrum of microbes and is packaged in a sterile, non-pyrogenic form. Independent claim 56 recites a lock flush composition comprising at least one of tri-sodium and tetra-sodium EDTA in solution at a concentration of at least 2.0% (w/v) and less than 15% (w/v) and having a pH of at least 9.5, wherein the antiseptic composition is packaged in a sterile, non-pyrogenic form and is biocompatible for use in in-dwelling access catheters, urinary catheters, nasal tubes and throat tubes.

Appellants' claimed antiseptic compositions and lock flush compositions are provided in a sterile and non-pyrogenic form and may be packaged in any convenient fashion. In some embodiments, antiseptic EDTA compositions of the

claimed subject matter may be provided in connection with or as part of a medical device, such as in a pre-filled syringe (Claim 46) or in a single dose vial (Claim 47). The compositions may be prepared under sterile, aseptic conditions, or they may be sterilized following preparation and/or packaging using any of a variety of suitable sterilization techniques.

The claimed compositions may be provided in a saline solution (claim 39), as well as in a solution comprising less than 10% (v/v) ethanol and water (claim 37). According to further embodiments of appellants' claimed compositions, the EDTA salt, or the combination of tri-sodium and tetra-sodium EDTA salt provides at least 50% of a total antimicrobial activity of the composition (claims 58 and 59, respectively).

VI. Grounds of Rejection to be Reviewed on Appeal

1) Claims 32, 34, 39, 41, 42, 45 and 55-60 stand rejected under 35 U.S.C. § 103(a) as being unpatentable over Fahim (WO 00/13656) in view of Wider (U.S. Patent No. 6,500,861).
2) Claim 47 stands rejected under 35 U.S.C. § 103(a) as being unpatentable over Fahim (WO 00/13656) in view of Wider (U.S. Patent No. 6,500,861) and further in view of *Root et al* ("Inhibitory Effect of Disodium EDTA upon the Growth of *Staphylococcus epidermidis* In Vitro: Relation to Infection Prophylaxis of Hickman Catheters").
3) Claim 46 stands rejected under 35 U.S.C. § 103(a) as being unpatentable over Fahim (WO 00/13656) in view of Wider (U.S. Patent No. 6,500,861) and further in view of Remington's Pharmaceutical Sciences.
4) Claims 32, 34, 37, 41, 42, 45 and 55-60 stand rejected under 35 U.S.C. § 103(a) as being unpatentable over Kurginski (GB 1 279 148) in view of Fahim (WO 00/13656) and Wider (U.S. Patent No. 6,500,861).

VII. Argument

1) § 103(a) – Fahim in view of Wider

Independent claims 32, 55, 56 and 57 and pending dependent claims 34, 39, 41, 42, 45, and 58-60 are finally rejected under 35 U.S.C. § 103(a) as being unpatentable over Fahim (WO 00/13656) in view of Wider (U.S. Patent No.

6,500,861). Appellants submit that the Examiner has not established a *prima facie* case of obviousness and this rejection must therefore be withdrawn.

Claims 32, 34, 39, 41, 42, 45, 55, 57 and 60

Claims 32, 34, 39, 41, 42, 45, 55, 57 and 60 are argued as a group with respect to patentability in view of the final rejection. Independent claim 57 recites antiseptic compositions comprising tri- and tetra-sodium EDTA in solution at a concentration sufficient to have antimicrobial activity, wherein the composition has a bactericidal effect over a broad spectrum of microbes, has a pH of at least 9.5, and is packaged in a sterile, non-pyrogenic form. Independent claims 32 and 55 recite similar subject matter and specify a concentration of at least 2.0% (w/v) and less than 15% (w/v) of an EDTA salt (at least one of tri- and tetra-sodium salt) in solution, wherein the composition has a bactericidal effect over a broad spectrum of microbes, has a pH of at least 9.5, and is packaged in a sterile, non-pyrogenic form.

Providing the claimed antiseptic compositions in a sterile, non-pyrogenic form is a significant feature. Because the claimed compositions are packaged in a sterile, non-pyrogenic form, they are safe for use in human health and veterinary applications and may be safe and biocompatible, at least in modest volumes, in a patient's bloodstream. Providing compositions packaged in a sterile, non-pyrogenic form typically requires special processing procedures for both packaging and solution components. These procedures are generally expensive and time consuming, and they may be subject to special regulations and approval by regulatory authorities. Care must be taken, for example, with regard to multiple potential sources for pyrogens, e.g., water used as a solvent or in processing, packaging components, raw materials, and equipment used. The time, effort and risk associated with providing compositions, such as the claimed antiseptic compositions, in a sterile, non-pyrogenic form are substantial.

Fahim discloses an antimicrobial **handwash** composition that may comprise tetra-sodium EDTA. The disclosure of Fahim suggests that the antimicrobial handwash compositions of Fahim are formulated and intended for use by employees in the food industry. The Examiner acknowledges that Fahim does not teach or suggest that the composition is packaged in a sterile, non-pyrogenic form. The exemplary compositions, formulation methodologies and animal testing protocols

described in Fahim do not disclose or suggest any sterility precautions or post-formulation sterilizing procedures. Appellants find no uses or proposed uses of the Fahim antimicrobial handwash compositions that would suggest providing the compositions of Fahim in a sterile, non-pyrogenic form would be necessary or advisable.

To remedy this deficiency of Fahim, the Examiner combines an isolated teaching from Wider with the handwash composition of Fahim. Applicants do not perceive any suggestion to combine the references in the manner proposed by the Examiner, or any motivation for doing so.

Wider discloses a fatty acid-based biocidal antimicrobial composition comprising an organic acid to maintain the composition at a pH below 5.0. The antimicrobial composition of Wider is intended for the treatment of microbial infections *of the body spaces and organs* of man or animals (*See, e.g.,* Col. 3, lines 59-65) and is administered as a liquid either orally or through a suitable delivery system, such as a catheter, an enema tube, needle or the like, or as a solid in tablet or encapsulated form. (*See, e.g.,* Col 4, lines 10-14.) Wider discloses an exemplary protocol for producing a composition that is sterile and pyrogen free (*See,* Example 1, Col. 7, lines 50-51) and discloses that peritoneal dialysis requires the use of sterile and pyrogen free fluids (*See*, Col. 6, lines 5-11). The compositions of Wider are disclosed as useful as an adjunct to peritoneal dialysis.

It is manifestly improper to piece together isolated teachings in the art in an attempt to meet the claimed subject matter. *In re Vaeck*, 947 F.2d 448, 20 USPQ2d 1438 (Fed. Cir. 1991) ("The teaching or suggestion to make the claimed combination and the reasonable expectation of success must both be found in the prior art and not based on Appellants' disclosure."). Here, the Examiner has done just this - improperly pieced together isolated teachings in the art without consideration for the invention as a whole, without consideration for whether one of ordinary skill in the art would be motivated to make the combination, and based on appellants' own disclosure.

Moreover, "it is the invention as a whole that must be considered in obviousness determinations. The invention as a whole embraces the structure, its properties and the problems it solves." *In re Wright*, 848 F.2d 1216 (Fed. Cir. 1988)." Accordingly, "casting an invention as a 'combination of old elements' leads

improperly to an analysis of the claimed invention by the parts, not by the whole." *Custom Accessories, Inc. v. Jeffery Allen Indus.*, 807 F. 2d 955 (Fed. Cir. 1987).

The claimed compositions are packaged in a sterile, non-pyrogenic form. Because the claimed compositions are packaged in a sterile, non-pyrogenic form, the claimed compositions are safe for use in human health and veterinary applications and may be safe and biocompatible, at least in modest volumes, in a patient's bloodstream. Thus, considering the claimed compositions as a whole, one skilled in the art would not modify the handwash of Fahim with the teachings of Wider to arrive at the claimed compositions. That is, one skilled in the art, aware of Wider's alleged teaching of antimicrobial compositions packaged in a sterile, pyrogen free form and designed for treatment of internal body spaces or organs, would not be motivated to modify a **handwash** composition to make it a sterile, pyrogen-free composition. There is simply no reason for one skilled in the art to package a handwash in a sterile, non-pyrogenic form because, for example, a handwash does not typically come into contact with a user in a manner where packaging in a sterile, non-pyrogenic form would be beneficial. A handwash composition is not intended for potential contact with a patient's bloodstream or to otherwise be possibly introduced into the patient's body. A handwash is simply meant to cleanse the skin.

However, the Examiner insists that one skilled in the art would be motivated to make the combination of Fahim and Wider in order to arrive at the presently claimed invention.

The alleged motivation to make this combination is that Wider allegedly teaches antimicrobial compositions that are packaged in a sterile and pyrogen free form and are used for eliminating infections from various surfaces, including the surface of the body. This is a mischaracterization of Wider and does not provide proper motivation to one skilled in the art to provide the antimicrobial handwash composition of Fahim in a sterile, non-pyrogenic form (see discussion, *supra*).

The Examiner's assertion that Wider teaches antimicrobial compositions for eliminating infection from the surface of the body is a mischaracterization because the applications of Wider are contemplated for contact with skin that is not normally exposed (i.e., broken, cut skin). As specifically disclosed in the passage beginning

at column 5, line 50, Wider teaches that the composition is for "internal spaces"[1] and expressly states:

> It is also contemplated that the present compositions be used for the elimination of microorganisms from exposed body tissues that ***normally are not exposed***, such as the skin and underlying structure exposed by trauma or incision for or during surgery, or because of the ***introduction of surgical instruments*** or other such devices, such as vascular catheters and the like. (Emphasis added).

This surgical application is the same application that the Examiner relies on (at column 6, line 53-55) to assert that Wider teaches antimicrobial compositions for eliminating infection from the surface of the body. Specifically, the application relied upon by the Examiner is a pre-surgical application of a composition. Thus, the application relied upon by the Examiner is for skin that is not normally exposed. One skilled in the art would not be motivated to modify a handwash based on the teachings of a composition that is for skin that is not normally exposed (i.e., broken, cut skin).

Moreover, Wider only recites specific applications of the composition wherein the composition should be in "sterile and pyrogen free" form. This application is for the treatment of "internal spaces." A specific application of the composition is as an adjunct to peritoneal dialysis where there is a risk of infection of the abdominal cavity. It is for this reason that Wider teaches at column 6, lines 5-11 (a passage relied on by the Examiner) that hypertonic dialysis fluid should be in "sterile and pyrogen free" form. Wider does not teach or suggest that other potential applications of the composition, such as an application that is not for the "internal spaces," should be in "sterile and pyrogen free" form. The Examiner cannot extrapolate such teachings from Wider. Statements of a prior art reference cannot be viewed in the abstract. Rather, they must be considered in the context of the teaching of the entire reference. See *In re Kotzab*, 208 F.2d 1352 (Fed. Cir. 2000). One skilled in the art reading Wider would understand that the composition would be in a sterile and pyrogen free form only because of the potential use on "internal spaces." That is, one skilled in the art would understand that Wider is not suggesting that a composition be placed in a sterile and pyrogen free form for other

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[1] "The term 'internal spaces' is meant to include, for example, the thorax, abdomen, gastrointestinal tract, urinary bladder, vagina, nasal sinuses, external auditory canal, urethra, and the like." Column 5, lines 52-55.

(non "internal spaces") purposes. Thus, Wider does not teach or suggest the use of a composition in a "sterile and pyrogen free" form for anything but the treatment of internal spaces. Accordingly, Wider is an isolated teaching of a composition in a "sterile and pyrogen free" form that is not applicable to a handwash that would *not* be used in "internal spaces." And, one skilled in the art would not be motivated to modify a handwash based on the teachings of a composition used for the treatment of internal spaces.

Accordingly, appellants assert that 1) Wider does not teach or suggest applications for normal state skin surfaces and 2) Wider only teaches a "sterile and pyrogen free" form for uses on "internal spaces."

Fahim, on the other hand, does not teach or suggest the use of a composition for the treatment or potential treatment of internal spaces. Fahim is simply focused on an antimicrobial **handwash** composition. See, e.g., Abstract and Field of Invention ("the invention relates to liquid antimicrobial handwash compositions"). Needless to state, a handwash composition is specifically designed to treat just the skin surfaces. For example, as may be seen from Example 11, when the composition of Fahim is placed in the eye of a rabbit, ocular irritation in the form of corneal opacity and conjunctivitis occurred.

Thus, the attempt of the Examiner to piece together an isolated teaching from Wider with the teachings of Fahim is devoid of proper consideration of the claimed invention as a whole and is made without the required suggestion to combine the references.

As discussed above, one skilled in the art would not modify a **handwash** composition to make it a sterile, pyrogen-free composition. There is no motivation to make such a modification found in the art. It is completely foreign and unnecessary to package a handwash composition in a sterile, non-pyrogenic form. There is no reason for one skilled in the art to package a handwash in a sterile, non-pyrogenic form because, for example, a handwash does not typically come into contact with a user in a manner where packaging in a sterile, non-pyrogenic form would be beneficial. A handwash composition is not intended for potential contact with a patient's bloodstream or to otherwise be possibly introduced into the "internal spaces" of a patient's body. A handwash is simply meant to cleanse the skin.

Moreover, one skilled in the art would not be motivated by the teaching of a sterile, pyrogen-free composition for "internal spaces" or body tissues that are normally not exposed to modify a **handwash** composition. To then undergo the extra time and expense to package a handwash in a sterile, non-pyrogenic form would not only not be obvious, it would actually be contrary to the teachings of Wider, which teach that the sterile and pyrogen free form should be used in applications on "internal spaces."

A further reason why it is improper to attempt to combine the teachings of Wider with those of Fahim is that Wider specifically requires a pH range of about 1.0 to about 5.0, preferably from about 2.5 to about 4.0. Column 4, lines 7-9 and 35-36. This range is several orders of magnitude from the pH recited in the claims on appeal (pH of at least 9.5) and is also substantially different from the pH of Fahim, which discloses a broad pH range of 5.0 to 11.0, preferably 5.5 to 10.5, and more preferably 7.5 to 9.5.

In this respect, it has long been established that it is impermissible under 35 U.S.C. § 103(a) to pick and choose from a reference only so much as will support a given position to the exclusion of other parts necessary to a full appreciation of what the reference fairly suggests to one of ordinary skill in the art. See *In re Wesslau*, 353 F.2d 238 (CCPA 1965). Yet, the Examiner has relied upon Wider without a full appreciation of what Wider fairly suggests to one of ordinary skill in the art. One of ordinary skill in the art would not rely on a reference with the pH range of Wider (1.0 to 5.0, preferably 2.5 to 4.0) to modify Fahim (pH range of 5.0 to 11.0, preferably 7.5 to 9.5) to arrive at the claims on appeal, which recite that the antiseptic composition has a pH of at least 9.5.

Accordingly, it is improper to attempt to combine the teachings of Wider with those of Fahim in order to arrive at the claims on appeal.

At best, the Board could take the position that it would be obvious to try the combination of prior art documents in the manner hypothesized in the Official Action. However, "obvious to try" is not the standard under 35 U.S.C. §103 as has been held by numerous decisions such as *In re Goodwin*, 198 USPQ 1 (CCPA 1978) and *In re Geiger*, 2 USPQ2d 1276 (Fed. Cir. 1987). All of these decisions have been previously discussed and appellants again assert their applicability without going into detail. Yet further, the positions taken by the Examiner in attempting to piece

together disparate teachings in the prior art are contrary to long standing decisions such as *In re Mercier*, 515 F.2d 1161, 1166, 185 USPQ 774, 778 (CCPA 1975) where the court reversed a prior art rejection stating: "The relevant portions of a reference include not only those teachings which would suggest particular aspects of an invention to one having ordinary skill in the art, but also teachings which would lead such a person away from the claimed invention."

Accordingly, the rejection of claims 32, 34, 39, 41, 42, 45, 55, 57 and 60 must be withdrawn.

Claim 56

The patentability of claim 56 is argued separately. Claim 56 specifies a lock flush composition comprising at least one of tri- and tetra-sodium EDTA in solution at a concentration of at least 2.0% (w/v) and less than 15% (w/v), having a pH of at least 9.5, packaged in a sterile, non-pyrogenic form, wherein the lock flush composition is biocompatible for use in in-dwelling catheters, urinary catheters, nasal tubes and throat tubes.

Appellants' arguments presented above with respect to the patentability of claims 32, 34, 39, 41, 42, 45, 55, 57 and 60 are reiterated with respect to the rejection of claim 56. Additionally, appellants submit that the combination of Fahim and Wider would *not* result in appellants' claimed lock flush composition. There is no suggestion that any composition of Fahim, even if it were packaged in a sterile, non-pyrogenic form, would be biocompatible for use in in-dwelling access catheters, urinary catheters, nasal tubes and throat tubes, as specified in claim 56. In fact, as mentioned previously, it is abundantly clear that the composition of Fahim, even if packaged in a sterile, non-pyrogenic form, would ***not*** be biocompatible for use in in-dwelling access catheters, urinary catheters, nasal tubes and throat tubes. Needless to state, a handwash composition is specifically designed to treat just the skin surfaces. There is no credibility in the assertion that the handwash composition of Fahim would be biocompatible for use in in-dwelling access catheters, urinary catheters, nasal tubes, or throat tubes. For example, as may be seen from Example 11, when the composition of Fahim is placed in the eye of a rabbit, ocular irritation in the form of corneal opacity and conjunctivitis occurred.

Neither Fahim nor Wider makes any suggestion to combine the teachings as proposed by the Examiner, and Appellants find no motivation to make any such combination. Furthermore, even if the combination were made, the combination does not result in the lock flush composition specified in appellants' claim 56. This rejection must be withdrawn.

Claims 58 and 59

The patentability of claims 58 and 59 is argued separately. Claims 58 and 59 are dependent and specify that the EDTA salt (claim 58) or the combination of tri- and tetra-sodium EDTA (claim 59) provides at least 50% of a total antimicrobial activity of the composition.

Appellants arguments presented above with respect to the patentability of claims 32, 34, 39, 41, 42, 45, 55, 56, 57 and 60 are reiterated with respect to the rejection of claims 58 and 59. The Examiner asserts that because Fahim discloses the same sodium salts of EDTA as are used in appellants' claims, the Fahim composition should possess the claimed properties (*See,* final rejection, page 6). Appellants respectfully traverse this rejection and submit the Examiner has not established a *prima facie* case of obviousness.

Fahim teaches a composition comprising three primary antimicrobial components: triclosan, PCMX (4-chloro-3,5-dimethyl phenol) and glutaraldehyde. An EDTA salt is not a required component, as is evident from the description of the first embodiment on page 5. Fahim teaches that EDTA or an EDTA salt (preferably tetra-sodium) may be added to the combination as an enhancer and allows formulation of a composition having a reduced amount of PCMX, improving the fragrance of the composition. (*See, e.g.,* page 10, lines 26-31.) It is evident that Fahim relies on the three primary components (triclosan, PCMX and glutaraldehyde) for the antimicrobial activity of the composition. Accordingly, Fahim does *not* teach or suggest that the EDTA salt, provided as an optional component in the antimicrobial combination composition, provides at least 50% of a total antimicrobial activity of the composition. And, based on the well-known and potent antimicrobial properties of the three primary components, triclosan, PCMX and glutaraldehyde, and the relative amounts of these primary components in the combination, it is

apparent that EDTA salt would not provide at least 50% of the total antimicrobial activity of the Fahim composition.

Neither Fahim nor Wider makes any suggestion to combine the teachings as proposed by the Examiner, and Appellants find no motivation to make any such combination. Furthermore, even if the combination were made, the combination does not result in the compositions set out in appellants' claims 58 and 59. This rejection must be withdrawn.

Conclusion

Accordingly, appellants respectfully request that the rejection of claims 32, 34, 39, 41, 42, 45, and 55-60 under § 103(a) as being obvious over Fahim in view of Wider, be withdrawn.

2) § 103(a) – Fahim in view of Wider and further in view of Root et al.

Claim 47 stands rejected under 35 USC § 103(a) as allegedly being obvious over Fahim (WO 00/13656) in view of Wider (US 6,500,861) and further in view of Root et al. Claim 47 depends from any of claims 32, 56 or 57 and further recites that the composition is in a single-dosage vial. This rejection is respectfully traversed.

The teachings of Fahim and Wider are described above with respect to the previous rejection. Appellants arguments presented above with respect to the patentability of claims 32, 34, 39, 41, 42, 45, 55, 56, 57 and 60 are reiterated with respect to the rejection of claim 47.

The Examiner concedes that Fahim does not specifically teach the antimicrobial composition in a single-dosage vial and further relies on the disclosure of Root et al. to motivate one of ordinary skill in the art to employ the handwash composition of Fahim in a sterile condition in a single-dosage vial.

Root et al. discloses the use of a di-sodium EDTA solution for inhibiting bacterial infection in intravenous catheters. During testing of the catheter flush solutions, the catheter flush solutions were inoculated with bacteria, incubated, and then centrifuged in sterile Eppendorf tubes. (*See*, Root et al., page 1628, lines 18-21, cited by the Examiner.) Sterile polystyrene test tubes were also used in some of Root et al.'s experimental protocols. Root et al. does not, however, overcome the

deficiencies of the combination of Fahim and Wider with respect to appellants' claimed antiseptic composition provided in a sterile, non-pyrogenic form in a single dosage vial, as specified by claim 47.

It would be absurd, unnecessary and prohibitively expensive to package the handwash composition of Fahim in a sterile condition in a single-dosage vial. Appellants submit that one of ordinary skill in the art would *not* be motivated by Root et al.'s use of sterile test tubes in experimental protocols to package the antimicrobial handwash composition of Fahim in a sterile, non-pyrogenic form in a single-dosage vial.

As stated above, it is manifestly improper to piece together isolated teachings in the art in an attempt to meet the claimed subject matter. Thus, the attempt to rely on Root et al., which relates to a catheter flush solution, to further modify the handwash composition of Fahim is improper. Reliance on Root et al. to provide a teaching of providing or motivation to provide the handwash composition of Fahim in a sterile, non-pyrogenic form in a single dosage vial is unfounded, is far outside the realm of obviousness, and could only be justified by improper resort to appellants' own specification and claims.

Accordingly, the Examiner has not set forth a proper *prima facie* case of obviousness and appellants respectfully request that the rejection of claim 47 under § 103(a) as being obvious over Fahim in view of Wider and further in view of Root et al. be withdrawn.

3) § 103(a) – Fahim in view of Wider and further in view of Remington's Pharmaceutical Sciences

Claim 46 stands rejected under 35 USC § 103(a) as being obvious over Fahim (WO 00/13656) in view of Wider (US 6,500,861) and further in view of Remington's Pharmaceutical Sciences. Claim 46 depends from any of claims 32, 56 or 57 and further recites that the composition is in a pre-filled syringe. This rejection is respectfully traversed.

The teachings of Fahim and Wider are described above with respect to the previous rejections. Appellants' arguments presented above with respect to the patentability of claims 32, 34, 39, 41, 42, 45, 55, 56, 57 and 60 are reiterated with respect to the rejection of claim 46.

The Examiner concedes that Fahim does not specifically teach the antimicrobial composition in a pre-filled syringe and further relies on the disclosure of Remington's Pharmaceutical Sciences to lead one of ordinary skill in the art to employ the antimicrobial composition of Fahim in a sterile condition in a pre-filled syringe.

Remington's Pharmaceutical Sciences teaches sterile, pyrogen free sodium chloride solutions for injection and hypodermic syringes for use for injection of liquids. The sodium chloride solution is disclosed to be an electrolyte replenisher administered intravenously. Remington's Pharmaceutical Sciences does not, however, lead one of ordinary skill in the art to provide appellants' claimed compositions in a sterile, non-pyrogenic form in a pre-filled syringe.

It would be absurd, unnecessary and prohibitively expensive to package the handwash composition of Fahim in a sterile condition in a pre-filled syringe. One skilled in the art would not be motivated by the teaching of a sterile, pyrogen-free electrolyte replenisher to modify a handwash. A handwash is not intended for potential contact with a patient's bloodstream or to otherwise be possibly introduced into a patient's body. A handwash is simply meant to cleanse the skin. Thus, there is no reason for one skilled in the art to package a handwash in a sterile, non-pyrogenic form because, for example, a handwash does not typically come into contact with a user in a manner where packaging in a sterile, non-pyrogenic form would be beneficial. One skilled in the art would not be motivated by a teaching of a sterile, pyrogen-free electrolyte replenisher to then undergo the extra time and expense to package a handwash in a sterile, non-pyrogenic form.

As stated above, it is manifestly improper to piece together isolated teachings in the art in an attempt to meet the claimed subject matter. Reliance on Remington's Pharmaceutical Sciences to provide a teaching or motivation to provide the handwash composition of Fahim in a sterile, non-pyrogenic form in a pre-filled syringe is unfounded, is far outside the realm of obviousness, and could only be justified by improper resort to appellants' own specification and claims.

Accordingly, the Examiner has not set forth a proper *prima facie* case of obviousness and appellants respectfully request that the rejection of claim 46 under § 103(a) as being obvious over Fahim in view of Wider and further in view of Remington Pharmaceutical Sciences, be withdrawn.

4) - § 103(a) – Kurginski in view of Fahim and in view of Wider

Claims 32, 34, 37, 41, 42, 45, and 55-60 stand rejected under 35 USC §103(a) as allegedly being obvious over Kurginski (GB 1 279 148) in view of Fahim (WO 00/13656) and in view of Wider (US 6,500,861). Appellants submit that the Examiner has not established a *prima facie* case of obviousness and this rejection must therefore be withdrawn.

Claims 32, 34, 37, 41, 42, 45, 55, 57 and 60

Claims 32, 34, 37, 41, 42, 45, 55, 57 and 60 are argued as a group with respect to patentability in view of the final rejection. The recitations of these claims have been summarized in connection with the previous rejection(s) and the teachings of the Fahim and Wider references have been discussed. The significance of providing of the appellants' claimed compositions in a sterile, non-pyrogenic form has also been emphasized.

Kurginski discloses "a cleaning composition useful for releasing the particular soils that tend to accumulate in toilets and similar sanitary facilities." Kurginski, page 1, lines 12-15. The soils to be cleaned include the "hard, rock-like, white or nearly white deposit, which is some kind of **reaction product from urine**, **adherent fecal matter**, ... and **rust**." *See, e.g.,* Kurginski, page 1, lines 25-60. The toilet cleaning composition of Kurginski comprises a lower alkanol, an alkanolamine, a mixture of two or more different lower alkyl ether alcohols and a chelator. Tetra-sodium EDTA is disclosed as a potential chelator for use in the compositions. While the composition of Kurginski may comprise tetra-sodium EDTA, it is improper to treat the composition of Kurginski as simply a generic composition which comprises tetra-sodium EDTA. It is a toilet cleaning composition.

The Examiner concedes that Kurginski does not teach its composition packaged in a sterile, non-pyrogenic form. The Examiner asserts that "It would have been obvious to a person of ordinary skill in the art to employ the compositions comprising sodium salts of EDTA [Kurginski] as antimicrobial compositions, as Fahim teaches that the compositions comprising tetra-sodium EDTA can be used as antimicrobial compositions." (*See*, Final Office Action of February 24, 2006, page 9.) The Examiner posits that because the two compositions have one constituent in

common, each may be used in the intended applications of the other. Thus, the Examiner proposes that one of ordinary skill in the art would be motivated to use the toilet cleaning composition (Kurginski) as an antimicrobial handwash composition (Fahim).

The composition of Kurginski is not simply a generic composition comprising sodium salts of EDTA that can be used/modified as any other composition that also comprises sodium salts of EDTA. The composition of Kurginski is a **toilet cleanser**. To establish a prima facie case of obviousness, the Examiner must find a suggestion in the art to combine teachings, or a motivation for one of ordinary skill in the art to combine teachings. The identification of one common constituent in disparate combination compositions used for different applications provides neither the requisite suggestion or motivation. That is, the Examiner must assert motivation to rely on a toilet cleanser to modify a handwash - and not just rely on a mischaracterization of Kurginski as a generic composition that comprises sodium salts of EDTA to modify another generic composition comprising tetra-sodium EDTA. The Examiner has not asserted a proper motivation to rely on a toilet cleanser to modify a handwash.

It is evident that the Examiner has improperly pieced together isolated teachings in the art without consideration for the invention as a whole. One skilled in the art would not be motivated to use the **toilet cleanser** of Kurginski, which is designed to treat rock-like deposits derived from urine, fecal matter and rust, for cleaning **skin**.

There is no motivation to adapt a toilet cleanser in a manner to arrive at the presently claimed invention.

Furthermore, appellants' claims recite antiseptic compositions having a bactericidal effect over a broad spectrum of microbes. There is no indication in Kurginski that the composition of Kurginski, optionally containing tetra-sodium EDTA, has any antimicrobial properties. Kurginski teaches, in fact, that when desired, a germicide can be added to the toilet cleaning composition to disinfect or sterilize surfaces. (See, e.g., Col. 3, lines 74-79.)

Even if one skilled in the art would be motivated to employ the toilet cleaning compositions of Kurginski as an antimicrobial handwash, there is no suggestion or motivation, whatsoever, to package the composition of Kurginski in a sterile, non-

pyrogenic form. There is no suggestion made in Kurginski, Fahim or Wider to combine the elements of the various references in the manner proposed by the Examiner, and there is no motivation for doing do. It would be absurd, unnecessary and prohibitively expensive, and would serve no purpose, to package the toilet cleanser of Kurginski in a sterile, non-pyrogenic form.

As pointed out above, the question under 35 U.S.C. 103(a) is not whether the differences between the claimed invention and the prior art would have been obvious, but whether the claimed invention as a whole would have been obvious. *Stratoflex, Inc. v. Aeroquip Corp.*, 713 F.2d 1530, 218 USPQ 871 (Fed. Cir. 1983); *Schenck v. Norton Corp.*, 713. F.2d 782, 218 USPQ 698 (Fed. Cir. 1983).

The attempt by the Examiner to piece together isolated teachings from Wider and Fahim to modify Kurginski in the manner proposed is devoid of proper consideration of the claimed invention as a whole and without proper consideration of the teachings of the prior art references as a whole. One skilled in the art would not be motivated to provide the **toilet cleanser** composition of Kurginski in a sterile, non-pyrogenic form.

There is no motivation to make such a modification found in the art. It is completely foreign and unnecessary to package a toilet cleanser composition in a sterile, non-pyrogenic form. There is no reason for one skilled in the art to package a toilet cleanser in a sterile, non-pyrogenic form because, for example, a toilet cleanser does not typically come into contact with a user, let alone in a manner where packaging in a sterile, non-pyrogenic form would be beneficial. A toilet cleanser composition is clearly not intended for potential contact with a patient's bloodstream or to otherwise be possibly introduced into the "internal spaces" of a patient's body. A toilet cleanser is simply meant to cleanse toilets. Thus, one skilled in the art would not be motivated by the teaching of a sterile, pyrogen-free composition to modify a **toilet cleanser** composition.

Additionally, the Examiner appears to rely on the combination of Fahim in view of Wider to attempt to remedy the substantial deficiencies of Kurginski, alleging that it would have been obvious to one skilled in the art to employ the composition of Fahim in a sterile, pyrogen-free condition because Wider allegedly teaches antimicrobial compositions packaged in a sterile, pyrogen-free form.

However, as addressed above, one skilled in the art would not have been motivated to incorporate the teachings of Wider into the composition of Fahim.

As discussed above, Fahim is focused on an antimicrobial handwash composition. To even attempt to combine this teaching with the toilet cleaning composition of Kurginski and the sterile, pyrogen-free composition of Wider would not be contemplated by those of ordinary skill in the art. Thus, there is no reason for one skilled in the art to package the toilet cleaning composition of Kurginski in a sterile, non-pyrogenic form even in view of the teachings of Fahim and Wider since there is no logical basis for packaging a toilet cleaning composition in a sterile, non-pyrogenic form.

Accordingly, the Examiner has not set forth a proper prima *facie case* of obviousness and this rejection must be withdrawn.

Claim 56

The patentability of claim 56 is argued separately. Claim 56 specifies a lock flush composition comprising at least one of tri- and tetra-sodium EDTA in solution at a concentration of at least 2.0% (w/v) and less than 15% (w/v), having a pH of at least 9.5, packaged in a sterile, non-pyrogenic form, wherein the lock flush composition is biocompatible for use in in-dwelling catheters, urinary catheters, nasal tubes and throat tubes.

Appellants' arguments presented above with respect to the patentability of claims 32, 34, 37, 41, 42, 45, 55, 57 and 60 are reiterated with respect to the rejection of claim 56. Additionally, appellants submit that the combination of Kurginski with Fahim and Wider would *not* result in appellants' claimed lock flush composition. There is no suggestion that any composition of Kurginski, even if it were packaged in a sterile, non-pyrogenic form, would be biocompatible for use in in-dwelling access catheters, urinary catheters, nasal tubes and throat tubes, as specified in claim 56. There is no credibility in the assertion that the composition of Kurginski, formulated to remove hard, rock-like, white or nearly white deposits, which are a reaction product from urine, adherent fecal matter and/or rust, would be biocompatible for use in in-dwelling access catheters, urinary catheters, nasal tubes and throat tubes.

Neither Kurginski nor Fahim nor Wider makes any suggestion to combine the teachings as proposed by the Examiner, and Appellants find no motivation to make any such combination. Furthermore, even if the combination were made, the combination does not result in the lock flush composition set out in appellants' claim 56. This rejection must be withdrawn.

Claims 58 and 59

The patentability of claims 58 and 59 is argued separately. Claims 58 and 59 are dependent and specify that the EDTA salt (claim 58) or the combination of tri- and tetra-sodium EDTA (claim 59) provides at least 50% of a total antimicrobial activity of the composition.

Appellants arguments presented above with respect to the patentability of claims 32, 34, 37, 41, 42, 45, 55, 56, 57 and 60 are reiterated with respect to the rejection of claims 58 and 59. The Examiner asserts that because Kurginski discloses the same sodium salts of EDTA as are used in appellants' claims, the Kurginski composition should possess the claimed properties (*See*, final rejection, page 10). Appellants respectfully traverse this rejection and submit that the Examiner has not established a *prima facie* case of obviousness.

Kurginski discloses a composition comprising a lower alkanol, an alkanolamine, a mixture of two or more different lower alkyl ether alcohols and a chelator. Tetra-sodium EDTA is disclosed as a potential chelator for use in the compositions. Indeed, Kurginski does not teach that EDTA salt alone has any antimicrobial properties and teaches that a germicide can be added to the composition to disinfect or sterilize the surfaces. *See*, Kurginski, page 3, lines 74-76.

Neither Kurginski nor Fahim nor Wider makes any suggestion to combine the teachings as proposed by the Examiner, and there is no motivation to make any such combination. Furthermore, even if the combination were made, the combination does not result in the appellants' claimed compositions, in which the EDTA salt provides at least 50% of a total antimicrobial activity of the composition. This rejection must be withdrawn.

Conclusion

Accordingly, appellants respectfully request that the rejection of claims 32, 34, 37, 41, 42, 45, and 55-60 under § 103(a) as being obvious over Kurginski in view of Fahim and in view of Wider, be withdrawn.

Conclusion

In view of the foregoing, further and favorable consideration of the pending claims in the form of a Notice of Allowance is respectfully requested.

Respectfully submitted,

Buchanan Ingersoll & Rooney PC

Date August 23, 2006

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Table of Contents

		Page
I.	Real Party in Interest	1
II.	Related Appeals and Interferences	1
III.	Status of Claims	1
IV.	Status of Amendments	1
V.	Summary of Claimed Subject Matter	1
VI.	Grounds of Rejection to be Reviewed on Appeal	3
VII.	Argument	3

VIII. CLAIMS APPENDIX

The Appealed Claims

1. – 31. (Canceled)

32. (Previously presented) An antiseptic composition comprising at least one salt of ethylene diamine tetraacetic acid (EDTA) in solution, wherein the at least one EDTA salt comprises at least one of tri-sodium and tetra-sodium EDTA at a concentration of at least 2.0% (w/v) and less than 15% (w/v), wherein the antiseptic composition has a bactericidal effect over a broad spectrum of microbes, wherein the antiseptic composition has a pH of at least 9.5, and wherein the antiseptic composition is packaged in a sterile, non-pyrogenic form.

33. (Canceled)

34. (Previously presented) A composition of either of claims 55 or 56, comprising tri-sodium and tetra-sodium EDTA.

35. – 36. (Canceled)

37. (Previously presented) A composition of any of claims 32, 56 or 57, wherein the solution comprises less than 10% (v/v) ethanol and water.

38. (Canceled)

39. (Previously presented) A composition of any of claims 32, 56 or 57, wherein the solution comprises saline.

40. (Canceled)

41. (Previously presented) A composition of any of claims 32, 55 or 57 formulated for topical application to surfaces and objects.

42. (Previously presented) A composition of any of claims 32, 55 or 57,

comprising tri- and tetra-sodium EDTA salts in an aqueous solution at a concentration of between 2.0% and 8.0% (w/v) EDTA salt(s).

43. - 44. (Canceled)

45. (Previously presented) A composition provided in a dry or partially hydrated formulation that, upon reconstitution with a solution, forms an antiseptic composition of any of claims 32, 56 or 57.

46. (Previously presented) A composition of any of claims 32, 56 or 57 in a pre-filled syringe.

47. (Previously presented) A composition of any of claims 32, 56 or 57 in a single-dosage vial.

48. – 54. (Canceled)

55. (Previously presented) An antiseptic composition comprising at least one salt of ethylene diamine tetraacetic acid (EDTA) in solution, wherein the at least one EDTA salt comprises at least one of tri-sodium and tetra-sodium EDTA at a concentration of at least 2.0% (w/v) and less than 15% (w/v), wherein the antiseptic composition has a bactericidal effect over a broad spectrum of microbes, wherein the antiseptic composition has a pH of at least 9.5, wherein the antiseptic composition is packaged in a sterile, non-pyrogenic form, wherein the solution is water, and wherein the antiseptic composition has an osmolarity of from 240-500 mOsM/Kg.

56. (Previously presented) A lock flush composition comprising at least one salt of ethylene diamine tetraacetic acid (EDTA) in solution, wherein the at least one EDTA salt comprises at least one of tri-sodium and tetra-sodium EDTA at a concentration of at least 2.0% (w/v) and less than 15% (w/v), wherein the lock flush composition has a pH of at least 9.5, wherein the lock flush composition is packaged in a sterile, non-pyrogenic form, and wherein the lock flush composition is

biocompatible for use in in-dwelling access catheters, urinary catheters, nasal tubes and throat tubes.

57. (Previously presented) An antiseptic composition comprising tri-sodium and tetra-sodium ethylene diamine tetraacetic acid (EDTA) in solution at a concentration sufficient to have antimicrobial activity, wherein the antiseptic composition has a bactericidal effect over a broad spectrum of microbes, wherein the antiseptic composition has a pH of at least 9.5, and wherein the antiseptic composition is packaged in a sterile, non-pyrogenic form.

58. (Previously presented) A composition of any of claims 32, 55 or 56, wherein the EDTA salt provides at least 50% of a total antimicrobial activity of the composition.

59. (Previously presented) A composition according to claim 57, wherein the combination of tri-sodium and tetra-sodium EDTA provides at least 50% of a total antimicrobial activity of the composition.

60. (Previously presented) A composition according to claim 57, wherein the concentration of tri-sodium and tetra-sodium EDTA in solution is at least 2.0% (w/v) and less then 15% (w/v).

IX. EVIDENCE APPENDIX

None

X. RELATED PROCEEDINGS APPENDIX

The Board is directed to an Appeal and associated Appeal Brief for U.S. Patent Application Serial No. 10/313,844, attached.

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Patent Application of	)	**Mail Stop:**
	)	**APPEAL BRIEF - PATENTS**
Peter KITE et al.	)	
	)	Group Art Unit: 1744
Application No.: 10/313,844	)	
	)	Examiner: Elizabeth L McKane
Filed: December 5, 2002	)	
	)	Confirmation No.: 8560
For: ANTI-MICROBIAL SYSTEMS AND METHODS	)	
	)	Appeal No.: 1

APPEAL BRIEF

Mail Stop APPEAL BRIEF - PATENTS
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Sir:

This appeal is from the decision of the Office issued on April 21, 2006, finally rejecting claims 7-17 and 21-24, which are reproduced as the Claims Appendix of this brief.

☒ A check covering the ☐ $250.00 (2402) ☒ $500.00 (1402) Government fee is filed herewith.

☐ Charge ☐ $250.00 (2402) ☐ $500.00 (1402) to Credit Card. Form PTO-2038 is attached.

The Commissioner is hereby authorized to charge any appropriate fees under 37 C.F.R. §§1.16, 1.17, and 1.21 that may be required by this paper, and to credit any overpayment, to Deposit Account No. 02-4800.

Table of Contents

		Page
I.	Real Party in Interest	1
II.	Related Appeals and Interferences	1
III.	Status of Claims	1
IV.	Status of Amendments	1
V.	Summary of Claimed Subject Matter	1
VI.	Grounds of Rejection to be Reviewed on Appeal	4
VII.	Argument	4

I. Real Party in Interest

The present application is assigned to Tyco Healthcare Group LP which is the real party in interest.

II. Related Appeals and Interferences

Appellants' legal representative and assignee do not know of any other appeal or interferences which will affect or be directly affected by or have a bearing on the Board's decision in the pending appeal. A Related Proceedings Appendix is attached.

III. Status of Claims

Claims 7-17 and 21-24 are pending, rejected and presently appealed. A copy of the claims involved in the appeal are contained in an attached Claims Appendix.

IV. Status of Amendments

No amendments have been filed subsequent to the final rejection of April 21, 2006.

V. Summary of Claimed Subject Matter

The presently claimed invention relates to methods for applying the disinfectant salts of ethylene diamine tetraacetic acid (EDTA) comprising tetrasodium EDTA in specific environments. See page 4, lines 4-11 and 19-22.

Infectious organisms often grow in biofilm systems that are commonly referred to as "slime". Such biofilms have a mechanical structure in addition to a chemical or biochemical structure. The effects of these biofilms on disinfectant agents, systems, and methods have not been well understood. Appellants believe that these biofilms function to protect at least some of the infectious organisms that form the biofilm. In particular, the biofilm can establish a protective "matrix" of glycocalyx, which induces a 'biofilm resistance phenotype', that protects the colonizing organisms within the biofilm by multiple up-regulation and down-regulation of genes. See page 4, line 23 to page 5, line 2.

Appellants have discovered that the disinfectant salts of EDTA of the present invention are relatively effective in treating undesirable biofilms because they help to

destroy the structure of the biofilm and allow the EDTA to kill or inhibit the growth of individual organisms within the biofilm. See page 5, lines 3-6.

It has been discovered that conduits can be treated with the tetrasodium salt of EDTA as a preventative antiseptic or as treatment following potential fungal or bacterial infection. See page 6, lines 23-25.

Typically, the disinfectant salts of EDTA, when used to treat conduits, are dissolved in water. See page 6, lines 26-27.

It has further been discovered that the stand-alone use of the tetrasodium salt of EDTA decontaminates and preserves potentially infected materials such as blood and plasma and conduits and containers therefor. See page 9, lines 3-10.

The treatment of catheters with the tetrasodium salt of EDTA falls under the general category of conduit treatment as described above, but is of particular significance. Catheter devices include all conduits that are used to deliver fluids into or remove fluids from the human body. A subcutaneous port is considered a catheter for the purposes of the present invention. See page 14, lines 17-22.

The tetrasodium salt of EDTA has been discovered to be an effective treatment for catheters defining an infected system. The tetrasodium salt of EDTA eradicates microbe colonization by killing an entire population of microbes when the catheter is treated with tetrasodium salt at a prescribed concentration using a liquid lock prior to and in between infusions and/or by surface coating of catheter devices. An application is the treatment of colonized or infected catheters by use of a liquid lock containing the tetrasodium salt of EDTA in the preferred concentration and pH. See page 14, line 23 to page 15, line 7.

Typically, the tetrasodium salt of EDTA, when used to treat catheters, is dissolved in water as a carrier, although other carriers may be used. Substances such as thrombolytics, sodium, alcohol, or reagents may also be added to the basic water/EDTA solution. See page 15, lines 8-11.

Appellants have tested the efficacy of the tetrasodium salt of EDTA against a number of microbes. The results of these tests are summarized in two tables attached to the specification as Exhibit A1 and A2[1]. See page 16, lines 8-10.

Exhibits A1 and A2 contain the results of laboratory tests in which six different

[1] The descriptions of Exhibits A1 & A2 were inadvertently switched in the original specification. This was corrected in Appellants' Amendment of April 7, 2005.

salts of EDTA were each tested against a variety of microbes from clinical isolates. Exhibit B contains a description of the test protocol used to obtain the conclusions set forth in the table of Exhibits A1 and A2, including a concentration of 10^6 organisms/mL in an EDTA broth. See page 16, lines 11-14.

While the numbers contained in the Exhibit A2 table identify the minimum concentration of each salt required to inhibit growth (MIC) of each of the tested microbes; the numbers contained in the Exhibit A1 table identify the minimum concentration of each salt required to kill an entire population (MBC) of each of the tested microbes; the concentration is expressed as milligrams of disinfectant salt per milliliters of water (mg/ml). Thus, for example, the MBC for *S. Epidermis* is 1 or 2 mg/mL using tetrasodium EDTA. See page 16 lines 15-22 and Exhibit A1[2].

Based on the test results as summarized in the Exhibit A1 and A2 tables, it can be seen that all of the tested salts are effective to some degree against all of the listed microbes. However, based on a balance of factors including material costs, minimum concentration required for inhibitory and bactericidal effect over a broad spectrum of microbes, material availability, and the like, Appellants conclude that tetrasodium EDTA demonstrates the most superior attributes. See page 17, lines 1-7.

Exhibit C provides a table summarizing the results of laboratory tests of clinical isolates in which three different salts of EDTA were each tested for bactericidal and inhibitory effect against a variety of yeasts. The protocol for agar dilution is described in Exhibit D appended to the specification. Page 17, lines 8-12.

Based on the test results as summarized in the Exhibit C table, it can be seen that the tetrasodium salt has both destructive and inhibitory effects against all of the listed yeasts. In particular, the Exhibit C table shows that the MIC values for tetra-sodium are lower than the MIC values for the other two EDTA compounds. The Exhibit C table shows that the MBC values for tetra-sodium EDTA are comparable to its MBC values for the Gram negative and Gram positive organisms. See page 17, lines 18-28.

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[2] Substitute Specification at page 12, lines 25-31.

VI. Grounds of Rejection to be Reviewed on Appeal

1) Claims 7-12, 14 and 21-24 stand rejected under 35 U.S.C. § 103(a) as being unpatentable over *Root et al* ("Inhibitory Effect of Disodium EDTA upon the Growth of Staphylococcus epidermidis In Vitro: Relation to Infection Prophylaxis of Hickman Catheters") in view of *Raad et al* (U.S. Patent No. 6,267,979).
2) Claims 13 and 15-17 stand rejected under 35 U.S.C. § 103(a) as being unpatentable over *Root et al* ("Inhibitory Effect of Disodium EDTA upon the Growth of Staphylococcus epidermidis In Vitro: Relation to Infection Prophylaxis of Hickman Catheters") in view of *Raad et al* (U.S. Patent No. 6,267,979) and further in view of Sodemann (U.S. Patent No. 6,166,007).

VII. Argument

Appellants' claims on appeal are directed to methods for disinfecting a conduit (claims 7-17) and methods for disinfecting a catheter (claims 21-24) using a disinfectant solution *consisting essentially of* an EDTA salt and a solvent, wherein the EDTA salt is at a concentration sufficient to have a *bactericidal effect over a broad spectrum of bacteria and a destructive effect against a variety of yeasts*, and wherein the EDTA salt comprises *tetrasodium EDTA*.

A "bactericidal effect," as disclosed and claimed by Appellants, is an effect that kills an entire population of bacteria, instead of simply just reducing or inhibiting their growth. The minimum concentration of a salt required to kill an entire population of each of the tested microbes is the MBC. A bactericidal effect is significant because disinfecting would have little practical utility if the methods exerted only an inhibitory or reducing effect and not a bactericidal effect. Contamination of conduits, e.g., catheters, poses serious and substantial health risks and bactericidal disinfection is a significant priority.

Thus, the claimed method involves disinfecting such that there is a bactericidal effect over a broad spectrum of bacteria and a destructive effect against a variety of yeasts.

Tetrasodium EDTA is a distinct chemical entity and is separate and different from other EDTA compositions, such as disodium EDTA. Tetrasodium EDTA is

unusually effective against a broad spectrum of bacteria and a variety of yeasts when used for disinfecting conduits and catheters. Thus, the identification of the bactericidal effects of tetrasodium EDTA is a significant advance.

Experimental Data

Appellants conducted tests on a broad spectrum of bacteria and variety of yeasts in support of Appellants' claims to methods for disinfecting conduits and catheters. The organisms used in Appellants' experiments are all clinical isolates and represent a broad spectrum of bacterial populations, many of which produce serious, even lethal infection if they are introduced into a patient's blood stream by means of a catheter or another medical device, or by means of fluids from contaminated conduits. The data were presented as Exhibits A1, A2 and C from the subject application at issue, and as Exhibit A, which was submitted with Appellants' January 24, 2006, Amendment. These Exhibits are attached to this Appeal Brief for the Board's convenience.

Exhibits A2 and A1 of the subject application, respectively, show the MIC (Minimum Inhibitory Concentrations) and MBC (Minimum Bactericidal Concentrations) of *tetrasodium EDTA* solutions (among others) required to inhibit growth (MIC) and kill (MBC) populations of numerous microorganisms including *S. Epidermis*.

Exhibit C of the subject application shows MIC and MBC experimental data for tetrasodium EDTA compositions against nine yeast populations.

Exhibit A shows data demonstrating the efficacy of tetrasodium EDTA compared directly to disodium EDTA which was generated and presented in Appellants' related application published June 10, 2004 as US 2004/0110841 A1 (*See*, e.g., Example 1 and Figs. 1A-1D). The data demonstrate significant differences in the ***bactericidal*** effect (measured as the MBC) of tetrasodium EDTA compared to the bactericidal effect of disodium EDTA on the same clinical isolates using the same experimental system. The data was generated using an agar dilution method in which various EDTA solutions and concentrations were introduced into the nutrient agar and the plates were inoculated with clinical isolate samples and allowed to incubate, followed by scoring of the plates for bacterial growth. Of the clinical isolates tested (for which data was available), there are fifteen (15) of thirty-

six (36) isolates for which the MBC of disodium EDTA is 50 mg/ml or more, and seven (7) in which the MBC of disodium EDTA is 100 mg/ml or more. In contrast, the MBC of tetrasodium EDTA for ***all*** of the isolates tested (for which data was available) was 40 mg/ml or less and for thirty-four (34) of the thirty-six (36) isolates tested, was 20 mg/ml or less including 1 or 2 mg/mL for *S. Epidermis*. In twenty one (21) of the thirty four (34) direct comparisons by Appellants between di- and tetrasodium EDTA, the MBC for disodium EDTA was more than twice the MBC exhibited by the tetrasodium EDTA.

The data clearly demonstrate the ***bactericidal*** effect of tetrasodium EDTA at the concentrations tested and claimed by Appellants, against a broad spectrum of bacteria. The data similarly highlight the unexpected effect of tetrasodium EDTA in comparison to the effects of disodium EDTA.

It is highly significant that tetra-sodium EDTA compositions were bactericidal against substantially all of the clinical bacterial isolates. Methods for disinfecting a conduit (claims 7-17) and disinfecting a catheter (claims 21-24) would have little practical utility if only some of the bacterial and yeast populations were eliminated, or if the methods exerted only an *inhibitory or reducing effect* and not a bactericidal effect. Appellants' data demonstrates that tetrasodium EDTA solutions, at the concentrations tested and claimed, have *a **bactericidal** effect over a **broad spectrum of bacteria**, and a destructive effect on a variety of yeasts*.

Root et al. in view of Raad et al.

The Examiner has alleged that claims 7-12, 14, and 21-24 are unpatentable over Root et al. in view of Raad et al.

Root et al., according to the Examiner, teaches a method for disinfecting a catheter by contacting the catheter with an aqueous EDTA solution in the form of a ***disodium salt*** having a concentration of 20 mg/ml. The Examiner alleges that Raad et al. teach that it is known in the art that both disodium and tetrasodium EDTA salts have a "significant growth inhibitory effect against species of fungal and bacterial microorganisms including Aspergillus, Fusarium, Candida, Psuedomonas, vancomycin-resistant enterococci, and multidrug resistant Stenotrophomonas." The Examiner concludes that it would have been obvious to one of ordinary skill in the art to substitute the tetrasodium salt of EDTA for the disodium salt employed by Root et

al. as both salts are disclosed to be suitable for use in methods of biofilm disruption.

The Examiner further alleges that because Root et al. disclose using a concentration of 20 mg/ml, the combination with Raad et al. will necessarily have an intrinsic "bactericidal effect over a broad spectrum of microbes and a destructive effect against a variety of yeasts." Appellants respectfully disagree and submit the following remarks.

Root et al.

The Root et al. model and teachings are specifically based upon the use of ***disodium EDTA*** [See Col. 1, paragraph 3]. The Root et al. authors note that microbiologists had previously studied the antibacterial action of ***disodium EDTA*** against various gram-negative organisms and that it has been used, ***in combination with other non-EDTA agents***, for gram-positive infections.

Root et al. worked specifically and exclusively with *disodium* EDTA and did not disclose or suggest that other EDTA salts may have similar properties or may be useful as disinfecting agents.

Root et al., according to the Examiner, discloses that, with respect to *S. Epidermis*, disodium EDTA causes at least a 1.5 log reduction in viable organisms even in the presence of catheter segments. The Examiner asserts that, "Thus, Root et al. actually teaches that disodium EDTA is indeed bactericidal, at least to an extent." However, this is incorrect as the Examiner has improperly interpreted the alleged teachings of Root et al.

A 1.5 log reduction is not a bactericidal effect, an effect that kills an entire population of bacteria. A 1.5 log reduction indicates that a significant number of bacteria remain and that there would be significant risk for bacterial contamination, such that the conduit is not disinfected. Thus, while Root et al. may teach disodium EDTA *inhibits* the growth of many bacterial organisms, Root et al. does not teach that the disodium EDTA composition has a ***bactericidal*** effect on the single strain of *S. epidermidis*.

Moreover, the method of the claims recites that the disinfectant solution contains an EDTA salt at a concentration sufficient to have a bactericidal effect over a ***broad spectrum*** of bacteria. Root et al. does not teach or suggest that disodium EDTA has a bactericidal effect over a broad spectrum of bacteria. A teaching of a

1.5 log reduction for a single species of bacteria is not a teaching of a bactericidal effect for a single species, let alone a broad spectrum of bacteria.

The Examiner attempts to rely on data from Appellants to assert that disodium EDTA has a bactericidal effect over a broad spectrum of bacteria. Appellants' data, and its results, are irrelevant in the manner it is relied upon by the Examiner. The Examiner must rely on what Root et al. teaches or suggests to one skilled in the art. Appellants' data is not part of that teaching.

In fact, Root et al. expressly teaches that disodium EDTA is unable to have a bactericidal effect in a variety of experiments for disinfecting catheters.

Table 1 in Root et al. shows the results of experiments in which solutions of disodium EDTA, heparin, Vancomycin and Vancomycin/heparin were applied on catheter surfaces 24 hours after inoculation with *S. epidermidis* (10^3 CFU), and the adherence and growth of *S. epidermidis* was measured after a 24 hour incubation period.[3] The results demonstrate that the Vancomycin and Vancomycin/heparin solutions effectively killed the bacterial populations, while significant bacterial populations remained on the catheter surfaces in contact with the disodium EDTA and heparin solutions. The catheter surface in contact with the disodium EDTA solution had a substantially lower bacterial population than the catheter surface in contact with the heparin solution, but *the bacterial population on the catheter surface contacted by disodium EDTA was significant and would pose a health threat.* (4)

The experimental results shown in Table 2 of Root et al. demonstrate that, of the disodium EDTA concentrations tested using an inoculation of 10^3 CFU *S. epidermidis*/ml, 20 mg/ml was the most effective concentration and *may have* prevented attachment of bacteria to the catheter. Nonetheless, a bacterial

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[3] As stated above, contamination of conduits poses serious and substantial health risks and bactericidal disinfection is a significant priority. Many bacterial populations may produce serious, even lethal infection if they are introduced into a patient's blood stream by means of a catheter or another medical device, or by means of fluids from contaminated conduits. A significant source of bacteria may be biofilms adhering to conduit surfaces. The efficacy of chemicals where biofilms are concerned is limited by the natural defense mechanisms of the embedded microorganisms. Planktonic or free-floating organisms may be readily destroyed by many chemical agents used to control microorganisms. But sessile, or fixed organisms located on conduit surfaces, are protected by a polysaccharide covering, or glycocalyx, and may have some success in warding off the effect of agents which destroy planktonic bacteria. An increased dose of agent may or may not succeed in overcoming the protection provided by this polysaccharide covering.

population was present in the culture medium 24 hours after inoculation. Appellants note, with respect to these data, that an inoculation of 10^3 CFU is very modest, and that experimental data generated using bacterial inoculations of 10^3 CFU would *not* provide scientifically or clinically convincing evidence that the solutions tested would be suitable for disinfecting conduits such as catheters. (5)

The data presented by Root et al. in Table 3 demonstrate that, with inoculations of 10^5 CFU *S. epidermidis*/ml, none of the disodium EDTA concentrations tested (up to 50 mg/ml) was effective to eliminate bacterial infections either on the catheter or in the medium. As succinctly stated on page 1630, column 1 of Root et al.: (6)

> EDTA was unable to maintain the catheter's sterility when faced with a 10^5 CFU/ml challenge.

These data show that using a disodium EDTA solution reduces the population of the tested *S. epidermidis* strain compared to using a heparin solution, but substantial bacterial populations persisted, both on catheter surfaces and in the culture medium. These data demonstrate that disodium EDTA at concentration ranges of 10-50 mg/ml, without an antimicrobial agent such as Vancomycin, would ***not*** be suitable for disinfecting conduits such as catheters.

Thus, one skilled in the art reviewing the experimental results of Root et al. would not be motivated to disinfect a catheter by contacting the catheter with a solution of disodium EDTA and solvent in order to achieve a bactericidal effect against even *S. epidermidis*, let alone a broad spectrum of bacteria.

Additionally, the Examiner has alleged that "The Root et al. reference illustrates the effect of increasing concentration on the effect of EDTA. Thus, one of ordinary skill in the art would have expected an increase in bactericidal effect with an increase in concentration."

This is incorrect.

There is no scientific basis for the Examiner's conclusion. An increased concentration may result in a greater inhibitory effect. But, the quantum leap of an increased concentration resulting in a bactericidal effect is unfounded. Indeed, Root et al. directly contradicts the Examiner's position by stating:

> EDTA was unable to maintain the catheter's sterility when faced with a 10^5 CFU/ml challenge. At very high concentrations, EDTA effected approximately a 3-log reduction in the number of

> viable bacteria. However, 1.5 $\log_{10}$ CFU/ml continued to thrive on the catheter surfaces after 24 h of incubation with 50 mg of EDTA per ml.

Root et al., page 1630, column 1.

The Examiner is requested to withdraw this assertion or provide scientific evidence to support the Examiner's conclusion.

Raad et al.

Raad et al., U.S. Patent 6,267,979, discloses control of biofouling in pipes in water treatment, pulp and paper manufacturing and oil field water flooding applications using compositions including the ***combination*** of a "*chelator*" *with an antimicrobial agent*. Raad et al. disclose that "chelators" have a significant growth *inhibitory effect* against species of fungal and bacterial microorganisms including those cited by the Examiner.

The present claims are directed to a disinfectant solution consisting essentially of an EDTA salt and a solvent. This specifically distinguishes other disinfectant solutions which have a disinfectant agent in addition to an EDTA salt. Raad et al. specifically teaches the ***combination*** of a chelator with a disinfectant (antimicrobial or fungicidal) agent. The thrust of the teachings of Raad et al., taken as a whole, is the alleged "synergistic inhibitory effect" produced by the ***combination*** of a chelator, such as EDTA, with an antibiotic or fungicidal agent. Accordingly, Appellants submit that the teachings of Raad et al. would *not* lead one of ordinary skill in the art to believe that a disinfectant solution consisting essentially of an EDTA salt and a solvent, wherein the EDTA salt comprises tetrasodium EDTA, would exert a bactericidal effect against a broad spectrum of bacteria.

Moreover, one skilled in the art would not be motivated to select tetrasodium EDTA from the chelators disclosed in Raad et al. to substitute for the disodium salt employed by Root et al. Tetrasodium EDTA is among the forty-four (44) "chelators" cited as *useful* in Table 1 of Raad et al. and among the forty-two (42) "chelators" described as *preferable* (*See*, Col. 3, line 59-Col. 4, line 18) ***for use in combination with one or more biocidal or antibiotic compounds***. Table 1 of Raad et al. is reproduced below for the Board's convenience:

Table 1- CHELATORS

ABBREVIATION	FULL NAME
EDTA free acid	Ethylenediamine-N,N,N',N',-tetraacetic acid
EDTA 2Na	Ethylenediamine-N,N,N',N',-tetraacetic acid, disodium salt, dihydrate
EDTA 3Na	Ethylenediamine-N,N,N',N',-tetraacetic acid, trisodium salt, trihydrate
EDTA 4Na	Ethylenediamine-N,N,N',N'-tetraacetic acid, tetrasodium salt, tetrahydrate
EDTA 2K	Ethylenediamine-N,N,N',N'-tetraacetic acid, dipotassium salt, dihydrate
EDTA 2Li	Ethylenediamine-N,N,N',N'-tetraacetic acid, dilithium salt, monohydrate
EDTA 2NH4	Ethylenediamine-N,N,N',N'-tetraacetic acid, diammonium salt
EDTA 3K	Ethylenediamine-N,N,N',N'-tetraacetic acid, tripotassium salt, dihydrate
Ba(II)-EDTA	Ethylenediamine-N,N,N',N'-tetraacetic acid, barium chelate
Ca(II)-EDTA	Ethylenediamine-N,N,N',N'-tetraacetic acid, calcium chelate
Ce(III)-EDTA	Ethylenediamine-N,N,N',N'-tetraacetic acid, cerium chelate
Co(II)-EDTA	Ethylenediamine-N,N,N',N'-tetraacetic acid, cobalt chelate
Cu(II)-EDTA	Ethylenediamine-N,N,N',N'-tetraacetic acid, copper chelate
Dy(III)-EDTA	Ethylenediamine-N,N,N',N'-tetraacetic acid, dysprosium chelate
Eu(III)-EDTA	Ethylenediamine-N,N,N',N'-tetraacetic acid, europium chelate
Fe(III)-EDTA	Ethylenediamine-N,N,N',N'-tetraacetic acid, iron chelate
In(III)-EDTA	Ethylenediamine-N,N,N',N'-tetraacetic acid, indium chelate
La(III)-EDTA	Ethylenediamine-N,N,N',N'-tetraacetic acid, lanthanum chelate
Mg(II)-EDTA	Ethylenediamine-N,N,N',N'-tetraacetic acid, magnesium chelate
Mn(II)-EDTA	Ethylenediamine-N,N,N',N'-tetraacetic acid, manganese chelate
Ni(II)-EDTA	Ethylenediamine-N,N,N',N'-tetraacetic acid, nickel chelate
Sm(III)-EDTA	Ethylenediamine-N,N,N',N'-tetraacetic acid, samarium chelate
Sr(II)-EDTA	Ethylenediamine-N,N,N',N'-tetraacetic acid, strontium chelate
Zn(II)-EDTA	Ethylenediamine-N,N,N',N'-tetraacetic acid, zinc chelate
CyDTA	trans-1,2-Diaminocyclohexane-N,N,N',N'-tetraaceticacid, monohydrate
DHEG	N,N-Bis(2-hydroxyethyl)glycine
DTPA-OH	1,3-Diamino-2-hydroxypropane-N,N,N',N'-tetraacetic acid
DTPA	1,3-Diaminopropane-N,N,N',N'-tetraacetic acid
EDDA	Ethylenediamine-N,N'-diacetic acid
EDDP	Ethylenediamine-N,N'-dipropionic acid dihydrochloride
EDDPO	Ethylenediamine-N,N'-bis(methylenephosphonic acid), hemihydrate
EDTA-OH	N-(2-Hydroxyethyl)ethylenediamine-N,N',N'-triacetic acid
EDTPO	Ethylenediamine-N,N,N',N'-tetrakis(methylenephosponic acid)
EGTA	O,O'-bis(2-aminoethyl)ethyleneglycol-N,N,N',N'-tetraacetic acid
HBED	N,N-bis(2-hydroxybenzyl)ethylenediamine-N,N-diacetic acid
HDTA	1,6-Hexamethylenediamine-N,N,N',N'-tetraacetic acid
HIDA	N-(2-Hydroxyethyl)iminodiacetic acid
IDA	Iminodiacetic acid
Methyl-EDTA	1,2-Diaminopropane-N,N,N',N'-tetraacetic acid
NTA	Nitrilotriacetic acid
NTP	Nitrilotripropionic acid
NTPO	Nitrilotris(methylenephosphoric acid), trisodium salt
O-Bistren	7,19,30-Trioxa-1,4,10,13,16,22,27,33-octaazabicyclo [11,11,11] pentatriacontane, hexahydrobromide
TTHA	Triethylenetetramine-N,N,N',N'',N''',N'''-hexaacetic acid

Moreover, tetrasodium EDTA is ***not*** among the four (4) chelators described as *most preferable* for use in combination with one or more biocidal or antibiotic compounds (EDTA free acid, EDTA 2Na, DTPA, and O-Bistren) (See column 4, lines 29-33).

Appellants observe that the identification of the "EDTA" solution used in Example 1 of Raad et al. for which data is presented in Figs. 1-4, 12, 13 and 14 is

unclear. The designation "EDTA" is used previously in the specification to refer to ethylenediamine-N,N,N',N'-tetraacetic acid (See, Col. 3, lines 60-61). This is the EDTA free acid presented in Table 1 and not one of the EDTA salts. The solutions used in Example 2 to demonstrate the fungicidal effect of the *combination* of an antifungal and a chelator, disodium EDTA (*See,* Col. 17, lines 6-9). Example 4 refers to the use of calcium disodium EDTA, disodium EDTA and "EDTA powder" for the preparation of a *combination* of minocycline + EDTA solution. Thus, it appears that Raad et al. did *not* use tetrasodium EDTA experimentally and it is clear that Raad et al. did *not* recognize tetrasodium EDTA as a powerful bactericidal composition.

Raad et al. disclose and demonstrate, at most, that chelators such as various EDTA compositions may have an ***inhibitory*** effect, and are only particularly effective when used in combination with a disinfectant agent. Thus, one skilled in the art reading Raad et al. would be ***taught away*** from using solely a chelator, such as EDTA, in the manner of the claimed method.

The Alleged Combination

Appellants' claims on appeal are directed to methods for disinfecting a conduit (claims 7-17) and methods for disinfecting a catheter (claims 21-24) using a disinfectant solution *consisting essentially of* an EDTA salt and a solvent, wherein the EDTA salt is at a concentration sufficient to have a *bactericidal effect over a broad spectrum of bacteria and a destructive effect against a variety of yeasts*, and wherein the EDTA salt comprises *tetrasodium EDTA*.

Root et al. teaches a method for disinfecting a catheter by contacting the catheter with an aqueous EDTA solution in the form of a **disodium salt** having a concentration of 20 mg/ml. However, Root et al. only teaches that the disodium salt has ***inhibitory*** effect against *S. epidermidis* in disinfecting catheter.

Raad et al. disclose and demonstrate, at most, that chelators such as various EDTA compositions may have an ***inhibitory*** effect, and are only particularly effective when used in combination with a disinfectant agent.

It is highly significant that the claimed methods provide a disinfectant solution that is bactericidal against substantially all of the clinical bacterial isolates and yeast populations tested. Methods for disinfecting a conduit (claims 7-17) and disinfecting

~~a catheter (claims 21-24) would have little practical utility if only some of the bacterial~~ and yeast populations were eliminated, or if the methods exerted only an inhibitory or reducing effect and not a bactericidal effect. The ***bactericidal*** effect of a disinfectant solution consisting essentially of an EDTA salt and a solvent, wherein the EDTA salt comprises *tetrasodium EDTA,* against a broad spectrum of bacteria and a variety of yeasts was disclosed and demonstrated by Appellants. This was unexpected in light of the prior art publications and the prior art references relied upon by the Examiner. Yet, the Examiner asserts that one skilled in the art would be motivated to arrive at the claimed method without any recognition in the cited art that tetrasodium EDTA solutions, at the concentrations tested and claimed, have *a* ***bactericidal*** *effect over a* ***broad spectrum of bacteria****, and a destructive effect on a variety of yeasts.* Instead, one skilled in the art would not be motivated to combine the teachings of Root et al. (inhibitory) with Raad et al. (inhibitory) to arrive at the claimed method which recites disinfecting such that there is a ***bactericidal*** effect over a broad spectrum of bacteria and a destructive effect against a variety of yeasts.

It is a basic principle that the Examiner bears the initial burden of establishing a *prima facie* case of obviousness. MPEP § 2142. When applying 35 U.S.C. 103, the following tenets of patent law must be adhered to:

(A) The claimed invention must be considered as a whole;

(B) The references must be considered as a whole and must suggest the desirability and thus the obviousness of making the combination;

(C) The references must be viewed without the benefit of impermissible hindsight vision afforded by the claimed invention; and

(D) Reasonable expectation of success is the standard with which obviousness is determined.

MPEP 2141 citing *Hodosh v. Block Drug Co., Inc.,* 786 F.2d 1135, 1143 n.5, 229 USPQ 182,187 n.5 (Fed. Cir. 1986). In this instance, the Examiner has not established a *prima facie* case of obviousness.

The mere fact that references *can* be combined or modified does not render the resultant combination obvious unless the prior art also suggests the desirability of the combination. MPEP § 2142. Here, the cited references do not suggest the

desirability of the combination.

Raad et al. states that chelators, generically, have a growth inhibitory effect against fungal and bacterial microorganisms and teach the ***combination*** of various chelators, including EDTA and various salts of EDTA, *with* known antimicrobial and antifungal agents, but in an environment totally different from the environment of Root et al. The teachings of Raad et al. are directed to this alleged combination and, taken in context, ***teach away*** from the claimed methods.

Furthermore, the teachings of Raad et al. are directed to the inhibitory effect of chelators rather than a bactericidal effect. Certainly had Raad et al. recognized that tetrasodium EDTA exerted a bactericidal effect, they would have made such a statement and would not have relied upon the effect of the combination of a chelator with a conventional antimicrobial agent. In fact, in further research, the Raad et al. authors continued to combine EDTA with antimicrobial agents in further research efforts. In a November 2003 publication, the Raad et al. authors teach that use of minocycline with EDTA "was significantly more effective" than using either compound or heparin by themselves[4]. One of the target organisms was S. epidermidis. The Raad et al. authors are ones skilled in the art, and yet they consistently did not recognize or use a solution that consisted essentially of an EDTA salt and a solvent.

Moreover, to arrive at something close to the claimed method, one would have to select tetrasodium EDTA from the list of forty-four (44) chelators disclosed in Table 1 of Raad et al., rather than the four chelators described as most preferable. But, there is nothing in the cited art that would have motivated persons skilled in the art to make such a selection and then to substitute it for the disodium salt employed by Root et al.

Accordingly, there is no teaching or suggestion in Raad et al. that *any* EDTA solution would be expected to, or does, exhibit a bactericidal effect over a broad spectrum of bacteria and a destructive effect against a variety of yeasts, much less the specifically claimed tetrasodium EDTA salt which has been shown to provide

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[4] Raad, Issam et al., "In Vitro and Ex Vivo Activities of Minocycline and EDTA Against Microorganisms Embedded in Biofilm on Catheter Surfaces," *Antimicrobial Agents and Chemotherapy*, Vol. 47, No. 11, pp. 3580-3585 (Nov. 2003). This article was considered by the Examiner, as indicated in the acknowledged citation form provided with the Office Action dated March 7, 2005.

superior results.

Root et al. worked specifically and exclusively with *disodium* EDTA and did not disclose or suggest that other EDTA salts may have similar properties or may be useful as disinfecting agents. Raad et al. does not teach or suggest that tetrasodium EDTA should be used alone.

Accordingly, one skilled in the art would not have been motivated to arrive at the presently claimed invention by selecting and substituting the tetrasodium EDTA of Raad et al. for the disodium EDTA employed by Root et al.

Additionally, one skilled in the art would not have looked to Raad et al. in order to modify the composition for disinfecting a catheter of Root et al.

The Examiner asserts it would have been obvious to one skilled in the art to modify the teachings of Root et al. in view of the teachings of Raad et al. However, Root et al. is focused on a catheter flush. Such a catheter flush may have potential contact with a patient's bloodstream or otherwise possibly be introduced into a patient's body. Raad et al., on the other hand, relates to controlling biofouling in "water treatment, pulp and paper manufacture and oil field flooding." See column 1, lines 13-15.

Thus, due to the distinct areas of technology, one skilled in the art would not have looked to Raad et al. in order to modify the composition for disinfecting a catheter of Root et al. One skilled in the art would not have been motivated to look to teachings in the fields of "water treatment, pulp and paper manufacture and oil field flooding" to modify a catheter flush. The Examiner is again impermissibly relying on Appellants' specification and claims as a basis for the combination. However, "The teaching or suggestion to make the claimed combination and the reasonable expectation of success must both be found in the prior art and not based on applicant's disclosure." See MPEP § 706.02(j) which cites *In re Vaeck*, 947 F.2d 488, 20 USPQ2d 1438 (Fed. Cir. 1991).

To place this point in further perspective, the Examiner's attention is directed to the decision in *In re Goodwin et al*, 198 USPQ 1 (CCPA 1978): In that case, one aspect of the invention was a method of manufacturing glass which used carbon monofluoride to provide relatively permanent lubrication. The Examiner had rejected the claims over two patents, one of which described a glass manufacturing method using lead compounds as lubricants and another (i.e., Margrave) which disclosed

carbon monofluorides useful as solid lubricants, but not in a glass manufacturing method. In addressing the rejection, the Court stated:

> At best, the PTO has shown evidence that it would have been obvious to the skilled artisan to try Margrave's carbon monofluorides. However, this Court has consistently refused to recognize "obvious to try" rejections. "As we have said many times, obvious to try is not the standard of 35 U.S.C. 103". (Citations omitted).

Thus, based on the same logic, Appellants respectfully submit that the proposed combination of Root et al. and Raad et al. is improper and even if proper, would not result in the claimed invention.

Appellants' claimed methods do *not* flow logically from the teachings of the prior art references relied upon for rejection and Appellants' invention as a whole is *not* obvious in light of these references, as alleged by the Examiner. There is no teaching or suggestion, in either Root et al. or Raad et al., that would lead one of ordinary skill in the art to combine the references in the way suggested by the Examiner to produce the claimed methods. Appellants perceive no motivation in either of the references to combine isolated aspects of the teachings of each reference to produce Appellants" claimed methods. Appellants also perceive no basis for a reasonable expectation of success if isolated aspects of the prior art references were combined in the manner suggested by the Examiner without the benefit of impermissible hindsight afforded by the teachings of Appellants" disclosure.

Accordingly, for the reasons stated above, Appellants respectfully submit that the combination of the teachings of Root et al. and Raad et al. does not teach or suggest the methods in the claims on appeal. Withdrawal of the rejection under 35 USC §103(a) is required.

Root et al. in view of Raad et al. further in view of Sodemann

Claims 13 and 15-17 are rejected under 35 U.S.C. §103(a) as being unpatentable over Root et al. in view of Raad et al., and further in view of Sodemann (U.S. Patent No. 6,166,007). This rejection is respectfully traversed, particularly in view of the remarks made herein.

The teachings of Root et al. and Raad et al. are discussed above. The Examiner alleges that Sodemann discloses the use of antimicrobial agents for

disinfecting other implanted devices such as various catheters and ports and that it would have been obvious to employ the method of Root et al. with Raad et al. to treat other implanted devices.

The Examiner relies on Sodemann for teaching disinfecting implanted devices such as catheters and ports, and for coating the exterior surfaces of catheters to prevent the deposition of blood coagula thereon and to thus prevent the growth of microbes (Col. 12, lines 44-58). Sodemann cites the Root et al. article as background research and uses an antimicrobial lock composition comprising at least one taurinamide derivative *in combination with* an acid or salt to produce a solution pH that is no higher than 7 [See Col 11, lines 30-60]. EDTA is listed as a potential acid and blood anticoagulant additive, and not as an antimicrobial. Although EDTA is listed as a potential anticoagulant, sodium citrate is preferred because of its pH lowering capability [See Col. 11, lines 30-60 and Col. 12, lines 24-43].

Sodemann does **not** remedy the deficiencies of Root et al. and Raad et al. with respect to the patentability of the claims on appeal. Appellants urge that no combination of the teachings of Root et al., Raad et al. and Sodemann would suggest methods for disinfecting a conduit using a disinfectant solution *consisting essentially of* an EDTA salt and a solvent, wherein the EDTA salt is at a concentration sufficient to have a *bactericidal* effect over a *broad spectrum of microbes* and a destructive effect against a variety of yeasts, and wherein *the EDTA salt comprises tetrasodium EDTA,* which has been shown to provide substantially superior results relative to *di*sodium EDTA. Instead, the additional reliance on Sodemann would at least further lead those of ordinary skill in the art to believe a separate antimicrobial agent is necessary.

Accordingly, for the reasons stated above, Appellants respectfully submit that the combination of the teachings of Root et al. and Raad et al. does not teach or suggest the methods in the claims on appeal. Withdrawal of the rejection under 35 USC §103(a) is required.

Respectfully submitted,

Buchanan Ingersoll PC

Date July 21, 2006

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VIII. CLAIMS APPENDIX

The Appealed Claims

1-6. (Canceled)

7. (Previously Presented) A method for disinfecting a conduit by contacting the conduit with a disinfectant solution consisting essentially of an ethylene diamine tetraacetic acid (EDTA) salt and a solvent, wherein the EDTA salt is at a concentration sufficient to have a bactericidal effect over a broad spectrum of bacteria and a destructive effect against a variety of yeasts, and wherein the EDTA salt comprises tetrasodium EDTA.

8. (Previously Presented) The method of claim 7, wherein the solvent is water.

9. (Previously Presented) The method of claim 7, wherein the concentration of the EDTA salt is from about 10 to about 80 mg for each ml of solvent.

10. (Previously Presented) The method of claim 7, wherein the concentration of the EDTA salt is more than 10 mg for each ml of solvent.

11. (Previously Presented) The method of claim 7, wherein contacting the conduit with the disinfectant solution is accomplished by locking, flushing or coating the conduit with the disinfectant solution.

12. (Previously Presented) The method of claim 7, wherein the conduit is a conduit carrying sterile fluids, blood, plasma, or water.

13. (Previously Presented) The method of claim 7, wherein the conduit is in an airway support device.

14. (Previously Presented) The method of claim 7, wherein the conduit is a catheter.

15. (Previously Presented) The method of claim 7, wherein the conduit is a port.

16. (Previously Presented) The method of claim 15, wherein the port is a subcutaneous port.

17. (Previously Presented) The method of claim 7, wherein the conduit is a urological catheter.

18-20. (Canceled)

21. (Previously Presented) A method for disinfecting a catheter comprising:

introducing a disinfectant solution into an interior lumen of the catheter, wherein the disinfectant solution consists essentially of an EDTA salt and a solvent, wherein the EDTA salt is at a concentration sufficient to have a bactericidal effect over a broad spectrum of bacteria and inhibitory effect against a variety of yeasts, and wherein the EDTA salt comprises tetrasodium EDTA;

holding the disinfectant solution within the lumen for a selected period of time; and

removing the disinfectant solution from the interior lumen.

22. (Previously Presented) The method of claim 21, wherein the EDTA salt is at a concentration sufficient to have a destructive effect against a variety of yeasts.

23. (Previously Presented) The method of claim 21, wherein the concentration of the EDTA salt is from about 10 to about 80 mg for each ml of solvent.

24. (Previously Presented) The method of claim 21, wherein the concentration of the EDTA salt is more than 10 mg for each ml of solvent.

25-33. (Canceled)

IX. EVIDENCE APPENDIX

Appellants have attached:

1) Exhibit A1 from the subject application at issue;

2) Exhibit A2 from the subject application at issue;

3) Exhibit C from the subject application at issue; and

4) Exhibit A, which was submitted with Appellants' January 24, 2006, Amendment.

EXHIBIT A

EXHIBIT A

EFFICACY OF DI- AND TETRA-SODIUM EDTA SOLUTIONS AGAINST VARIOUS CLINICAL ISOLATES

Organism ID	Di-sodium EDTA		Tetra-sodium EDTA	
	MIC	MBC	MIC	MBC
S24 Staph. epidermidis	<0.5	<0.5	<0.5	<0.5
31 Staph. epidermidis	<0.5	<0.5	<0.5	<0.5
301 Staph. xylosus	<0.5	<0.5	<0.5	20
300 Staph.capitis	<0.5	<0.5	<0.5	10
J46 Staph.lentus	<0.5	<0.5	<0.5	<0.5
S24 Staph.capitis	<0.5	<0.5	<0.5	<0.5
R8 Staph. simulans	<0.5	1	<0.5	1
72 S.aureus	<0.5	<0.5	<0.5	<0.5
R57 S.aureus	<0.5	10	<0.5	8
R13 S.aureus	<0.5	10	<0.5	<0.5
R30 S.aureus	<0.5	10	------	-------
8 S.aureus	<0.5	<0.5	------	------
R64 MRSA	<0.5	<0.5	<0.5	<0.5
R51 MRSA	<0.5	1	<0.5	<0.5
R92 MRSA	<0.5	10	<0.5	<0.5
S93 MRSA	<0.5	<0.5	<0.5	<0.5
J67 MRSA	<0.5	10	<0.5	<0.5
R8 VRE	<0.5	100	<0.5	30
Woods VRE	<0.5	100	<0.5	1
S77 Enterococcus Faecium	<0.5	100	<0.5	6

Organism ID	Di-sodium EDTA		Tetra-sodium EDTA	
	MIC	MBC	MIC	MBC
S76 Enterococcus faecalis	<0.5	100	<0.5	40
68 Klebsiella pneumoniae	8	60	6	6
R51 Klebsiella pneumoniae	-----	-----	------	-----
128 Klebsiella oxytoca	1	90	4	6
J7 Klebsiella ornitholytica	1	60	4	8
250 E. coli	1.5	80	1.5	1.5
B/C E. coli	-----	-----	------	-----
137 E. coli	4	60	2	2
292 Ent. cloacae	4	>100	6	15
190 Ent. cloacae	4	100	6	15
J22 Ent. cloacae	6	>100	6	10
R4 Steno. maltophilia	-----	-----	-----	-----
B/C Pseudomonas aeruginosa	-----	-----	-----	-----
J20 Pseudomonas aeruginosa	<0.5	50	2	4
J26 Pseudomonas sp.	<0.5	25	8	4
R75 Coryne. amycolatum	NG	NG	<0.5	20
R23 Coryne. strait/amy	NG	NG	<0.5	<0.5
177 Acinetobacter baumanii	<0.5	<0.5	<0.5	<0.5
J44 Acinetobacter baumanii	<0.5	1	<0.5	<0.5

Organism ID	Di-sodium EDTA		Tetra-sodium EDTA	
	MIC	MBC	MIC	MBC
R16 Proteus mirabilis	<0.5	50	<0.5	15
R81 Proteus vulgaris	<0.5	15	<0.5	8
R26 Proteus mirabilis	<0.5	50	1	15

EXHIBIT A1

EXHIBIT A1

Organism	Cupric disodium EDTA	Dipotassium EDTA	Diammonium EDTA	Tetrasodium EDTA	Magnesium disodium EDTA	Ferric-sodium salt EDTA
S. epidermidis	<0.5	8	4	1	30	>30
S.epidermidis	<0.5	8	8	2	30	>30
S.xylosus	<0.5	6	4	25	>30	>30
S. capitis	<0.5	10	8	6	>30	>30
S.lentus	<0.5	10	10	30	>30	>30
S. capitis	<0.5	8	10	>30	>30	>30
S. simulans	<0.5	8	10	30	>30	>30
S.aureus	<0.5	6	6	30	>30	>30
S.aureus	<0.5	8	10	>30	>30	>30
S.aureus	<0.5	6	15	>30	>30	>30
S.aureus	<0.5	8	15	<0.5	>30	>30
S.aureus	<0.5	8	10	8	>30	>30
MRSA	<0.5	6	8	8	>30	>30
MRSA	<0.5	10	6	10	>30	>30
MRSA	<0.5	8	>15	>30	>30	>30
MRSA	<0.5	8	10	30	>30	>30
MRSA	<0.5	8	10	25	>30	>30
VRE	<0.5	8	15	15	>30	>30
VRE	>30	8	>15	>30	>30	>30
Ent. faecuim	<0.5	8	15	>30	>30	>30
Ent. faecalis	<0.5	15	15	10	>30	>30
Kleb. pnemoniae	>30	15	>10	15	>30	>15
Kleb. pnemoniae	>30	15	>10	15	>30	>15

Kleb. oxytoca	>30	15	>10	8	>30	>15
Kleb. ornitholytica	>30	>15	>10	30	>30	>15
E.coli	>30	>15	>10	10	>30	>15
E. coli	>30	15	>10	1.5	>30	>15
E. coli	>30	15	>10	10	>30	>15
Ent. cloacae	>30	15	>10	20	>30	>15
Ent. cloacae	>30	>15	>10	20	>30	>15
Ent. cloacae	8	>15	>10	20	>30	>15
Steno. maltophilia	>30	10	>10	4	>30	>15
Pseudomonas aeruginosa	>30	>15	>10	20	>30	>15
Pseudomonas aeruginosa	>30	>15	>10	20	>30	>15
Pseudomonas sp.	>30	15	>10	30	>30	>15
Cornyeform amycolatum	<0.5	<0.5	1	<0.5	4	10
Coryneform strait/amy	<0.5	<0.5	1	<0.5	4	10
Acinetobacter baumanii	<0.5	<0.5	<0.5	<0.5	<0.5	10
Acinetobacter baumanii	15	>15	>10	2	>30	>15
Proteus mirabilis	>30	>15	>10	20	>30	>15
Proteus vulgaris	>30	>15	>10	20	.30	>15
Proteus mirabilis	>30	15	>10	20	>30	>15

EXHIBIT A2

EXHIBIT A2

Organism	Cupric disodium EDTA	Dipotassium EDTA	Diammonium EDTA	Tetrasodium EDTA	Magnesium disodium EDTA	Ferric-sodium salt EDTA
S. epidermidis	<0.5	<0.5	<0.5	1	6	>20
S.epidermidis	<0.5	<0.5	<0.5	1	6	>20
S.xylosus	<0.5	<0.5	<0.5	<0.5	2	>20
S. capitis	<0.5	<0.5	<0.5	<0.5	1.5	>20
S.lentus	<0.5	<0.5	<0.5	1	6	>20
S. capitis	<0.5	<0.5	<0.5	1	6	>20
S. simulans	<0.5	<0.5	<0.5	1	1.5	>20
S.aureus	<0.5	1	1	<0.5	>30	>20
S.aureus	<0.5	1	1	1	>30	>20
S.aureus	<0.5	1	1	1	>30	>20
S.aureus	<0.5	1	1	1	>30	>20
S.aureus	<0.5	1	1	<0.5	>30	>20
MRSA	<0.5	1	1	1	>30	>20
MRSA	<0.5	1	1	1	>30	>20
MRSA	<0.5	1	1	1	>30	>20
MRSA	<0.5	1	1	1	>30	>20
MRSA	<0.5	1	1	1	>30	>20
VRE	<0.5	<0.5	<0.5	1	25	2
VRE	>30	1	1	1	>30	>20
Ent. faecuim	<0.5	<0.5	<0.5	<0.5	1.5	4
Ent. faecalis	<0.5	1	1	1	>30	4
Kleb. pnemoniae	>30	1.5	4	8	>30	>15

Kleb. pnemoniae	>30	1	1.5	4	>30	15
Kleb. oxytoca	>30	1	1	4	>30	>15
Kleb. ornitholytica	>30	1	1	4	>30	15
E.coli	>30	1	1	4	>30	15
E. coli	6	1	1.5	1	>30	>15
E. coli	>30	1	4	4	>30	>15
Ent. cloacae	>30	4	4	8	>30	>15
Ent. cloacae	>30	4	4	10	>30	>15
Ent. cloacae	6	6	<0.5	8	>30	>15
Steno. maltophilia	6	<0.5	1	1	>30	10
Pseudomonas aeruginosa	>30	1	1	2	>30	15
Pseudomonas aeruginosa	>30	1	1	2	>30	15
Pseudomonas sp.	>30	1	<0.5	2	>30	15
Cornyeform amycolatum	<0.5	<0.5	<0.5	<0.5	<0.5	10
Coryneform strait/amy	<0.5	<0.5	<0.5	<0.5	<0.5	10
Acinetobacter baumanii	<0.5	<0.5	<0.5	<0.5	<0.5	6
Acinetobacter baumanii	6	<0.5	<0.5	1	>30	>15
Proteus mirabilis	6	<0.5	<0.5	1	>30	>15
Proteus vulgaris	>30	1	<0.5	4	>30	>15
Proteus mirabilis	6	<0.5	<0.5	1	>30	>15

EXHIBIT C

EXHIBIT C

Organism	Di-ammonium EDTA (MIC's)	Di-ammonium EDTA (MBC's)*	Di-potassium EDTA (MIC's)	Di-potassium EDTA (MBC's)*	Tetra-sodium EDTA (MIC's)	Tetra-sodium EDTA (MBC's)
C. albicans	0.5	ND	0.5	ND	0.5	15
C. albicans	0.5	ND	0.5	ND	0.5	15
C. albicans	0.5	ND	0.5	ND	0.5	0.5
C. lucitaniae	0.5	ND	0.5	ND	0.5	6
C. tropicalis	1	ND	1	ND	0.5	10
C. guilliermondii	0.5	ND	0.5	ND	0.5	0.5
C. glabrata	0.5	ND	0.5	ND	0.5	2
C. parapsilosis	0.5	ND	0.5	ND	0.5	8
C. glabrata	0.5	ND	0.5	ND	0.5	8

* Unable to perform > 0.1 mg/mL as agar was dissolved by agent

X. RELATED PROCEEDINGS APPENDIX

None.